

5-2019

# “-itis & -itis”: Immune Checkpoint Inhibitors Toxicity Management

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# “-itis & -itis”: IMMUNE CHECKPOINT INHIBITORS TOXICITY MANAGEMENT

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May 31, 2019

# Disclosure

- Speakers' Bureau: BMS, Merck.
- Advisory Meetings: Abbvie, Genentech.

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# Objectives

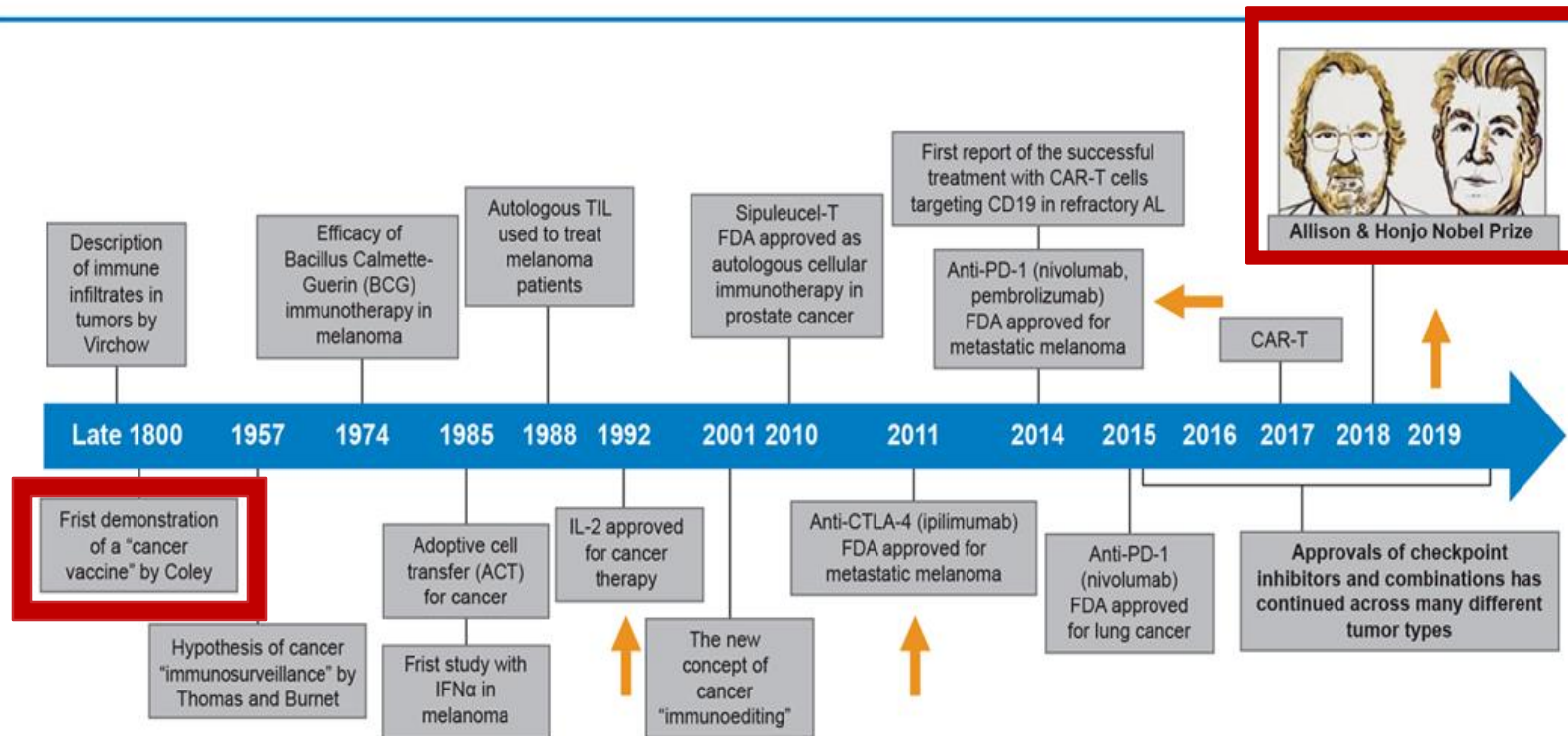
- Learn immune checkpoint inhibitor's (immunotherapy) mechanism of action.
- Recognize the differences in immunotherapy side effects vs chemotherapy side effects.
- Learn initial management of immunotherapy side effects.
- Learn about the resources available for immunotherapy side effect management.

St. Joseph Hospital and Health Center | Cancer Care

# What is Immunotherapy?

- A type of therapy that affects the immune system to fight cancer.
- Many different types of immunotherapy: vaccines, small molecule compounds, monoclonal antibodies, gene therapies, cellular therapies.
- For the purpose of this talk, I will use the terms “Immunotherapy” and “Immune Checkpoint Inhibitors” interchangeably.

# Key Milestones in the Evolution of Cancer Immunotherapy



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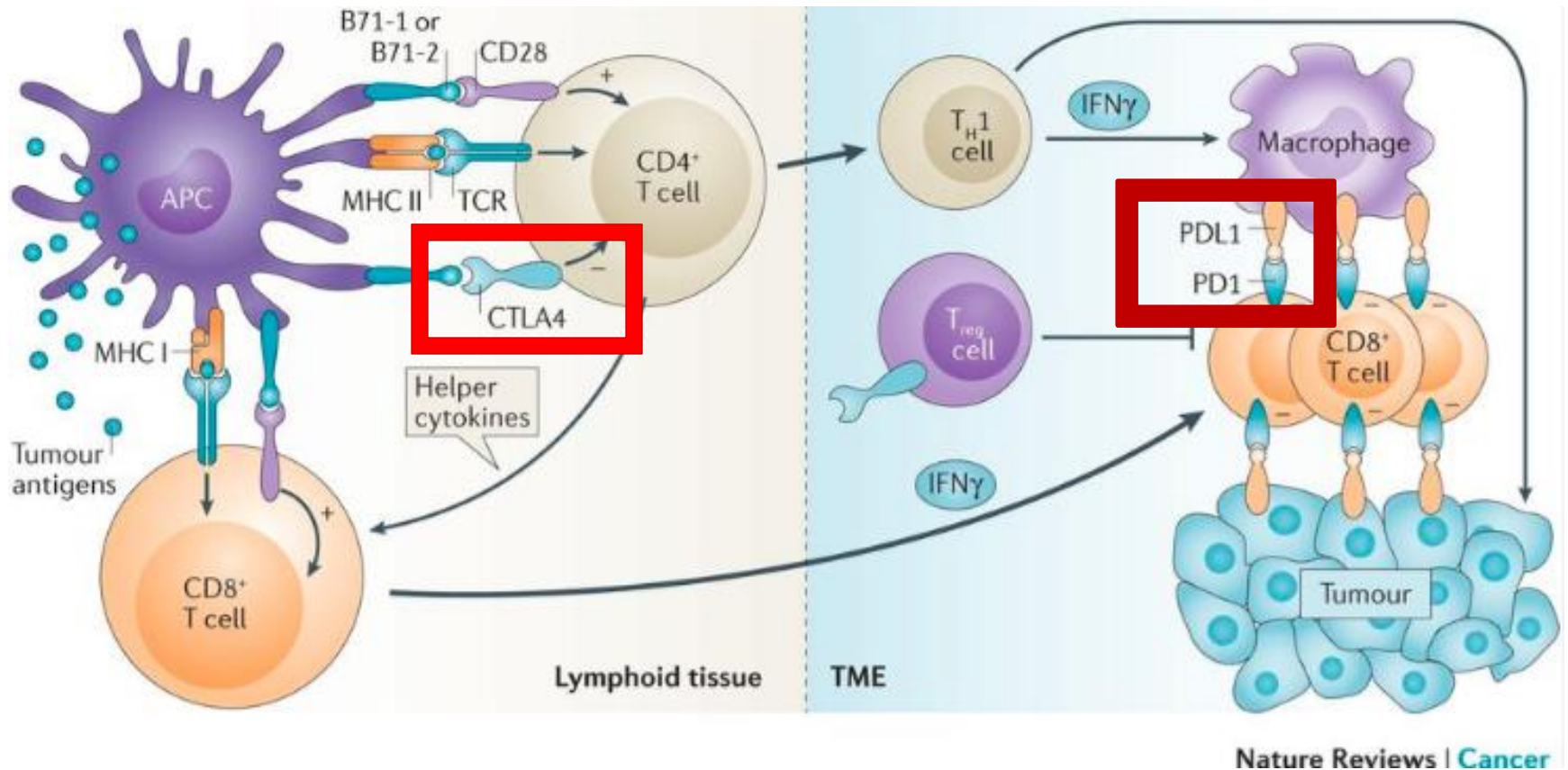
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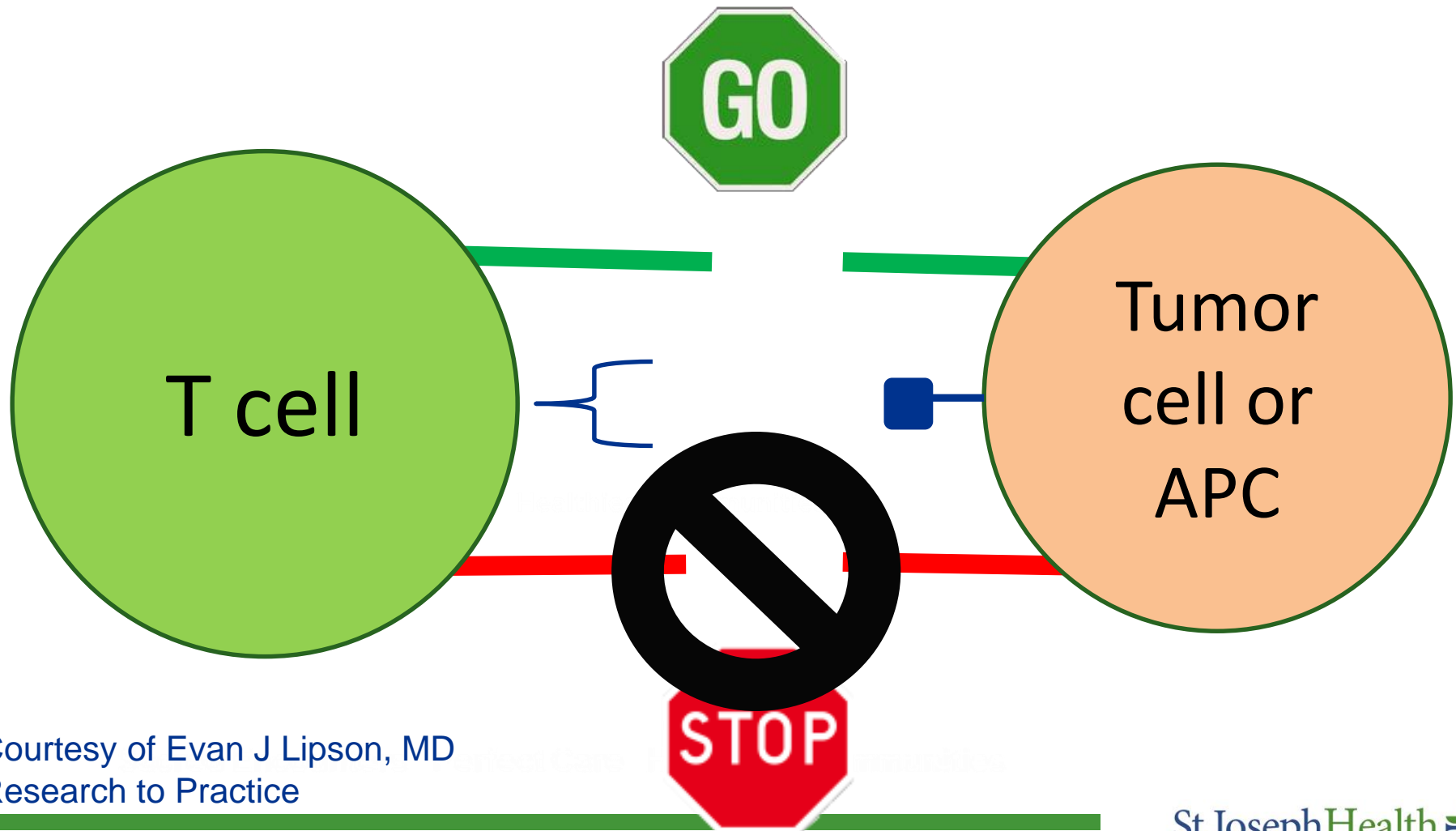
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# Immune Checkpoint Inhibitor Mechanisms of Action



Suzanne L. Toaplian, et al. *Nature Reviews Cancer* **volume 16**, pages 275–287 (2016)

# Immune Checkpoint Blockade: Mechanism of Action



Courtesy of Evan J Lipson, MD  
Research to Practice



# FDA approved Agents and Indications

- Ipilimumab (CTLA-4 ab)
- Cemiplimab-rwlc, Nivolumab, Pembrolizumab (PD-1 ab)
- Atezolizumab, Avelumab, Durvalumab (PD-L1 ab)
- More than 30 FDA approved Indications across multiple cancer types, and GROWING!

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# Immunotherapy is better tolerated



Chemotherapy



Immunotherapy

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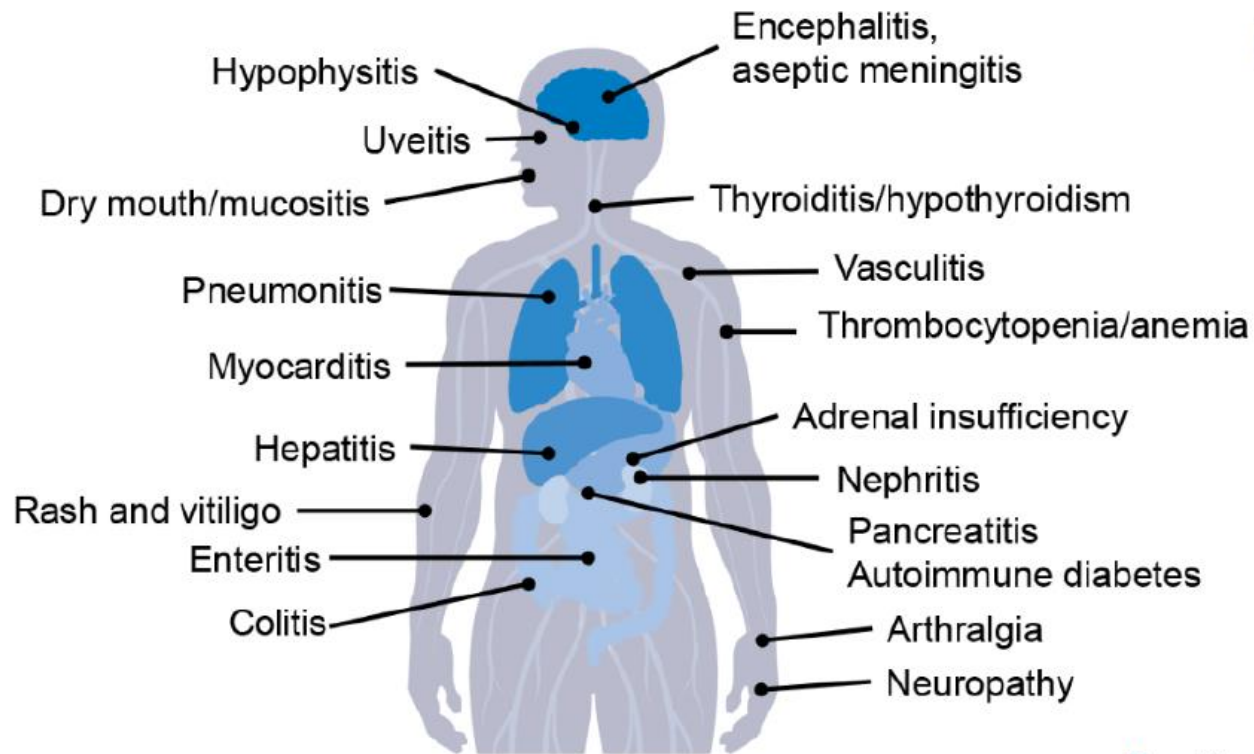
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# Severe Side Effects are Rare but Do Occur

Variable	Anti-CTLA-4 (n = 5368)	Anti-PD-1 (n = 9136)	Anti-PD-L1 (n = 3164)	Anti-PD-1/PD-L1 Plus CTLA-4 (n = 1549)
Deaths, No. (%)	58 (1.08)	33 (0.36)	12 (0.38)	19 (1.23)
Type of fatal toxic effect				
Colitis	23 (40)	2 (6)	0	2 (11)
Pneumonitis	3 (5)	14 (42)	5 (42)	4 (21)
Hepatitis	5 (9)	0	1 (8)	2 (11)
Cardiac	9 (16)	4 (12)	3 (25)	4 (21)
Neurologic	1 (2)	1 (3)	0	3 (16)
Nephritis	1 (2)	0	0	1 (5)
Hematologic	2 (4)	2 (6)	0	2 (11)
Infectious	8 (14)	5 (15)	2 (18)	3 (16)
Hemorrhagic/thrombotic	2 (4)	1 (3)	0	1 (5)
Electrolyte imbalance	1 (2)	2 (6)	0	0
Multiorgan failure	3 (5)	0	0	0
Other	1 (2)	2 (6)	1 (8)	0

*JAMA Oncol.* 2018;4(12):1721-1728.

# Immune side effects can involve Any Organ

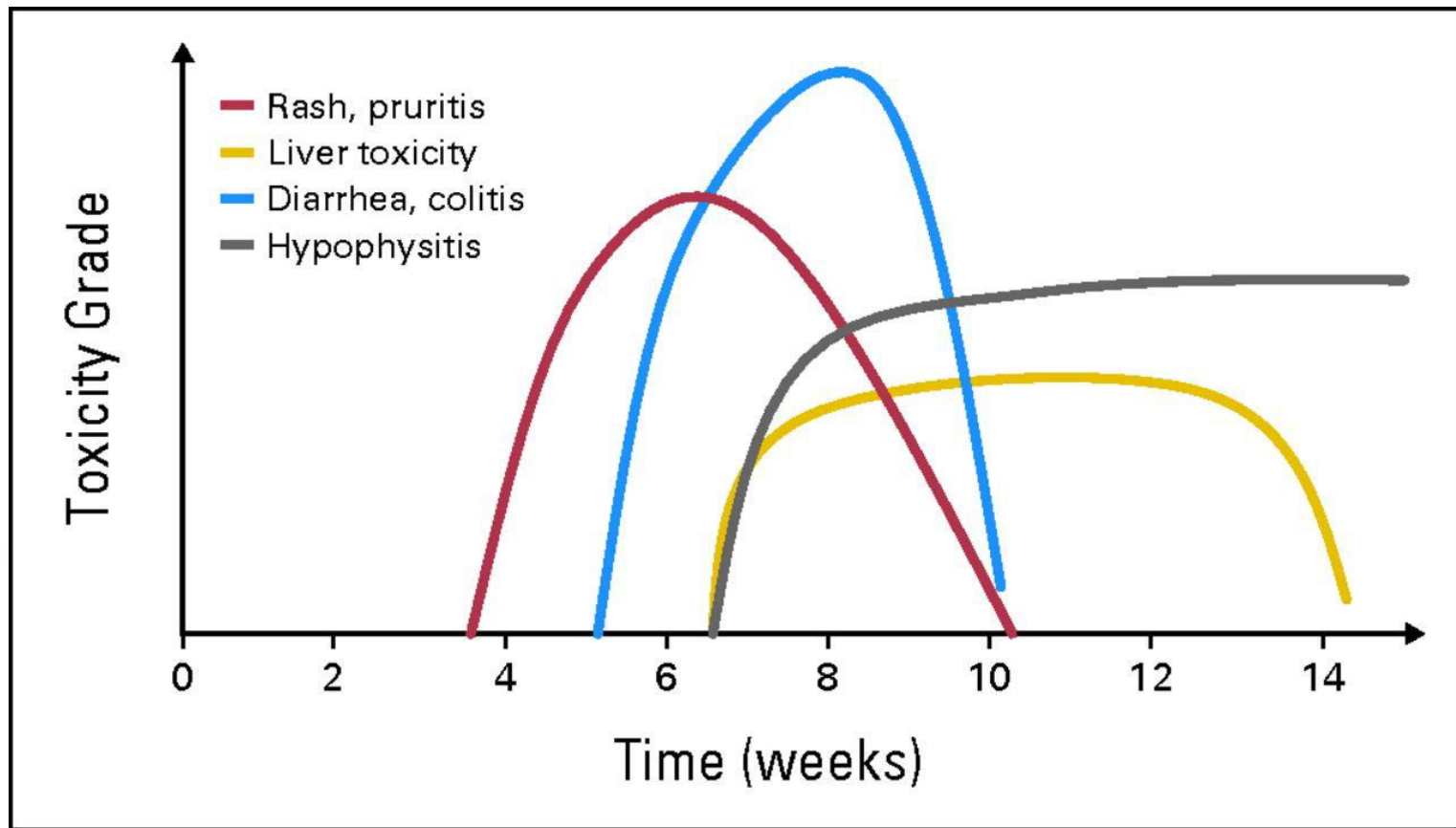


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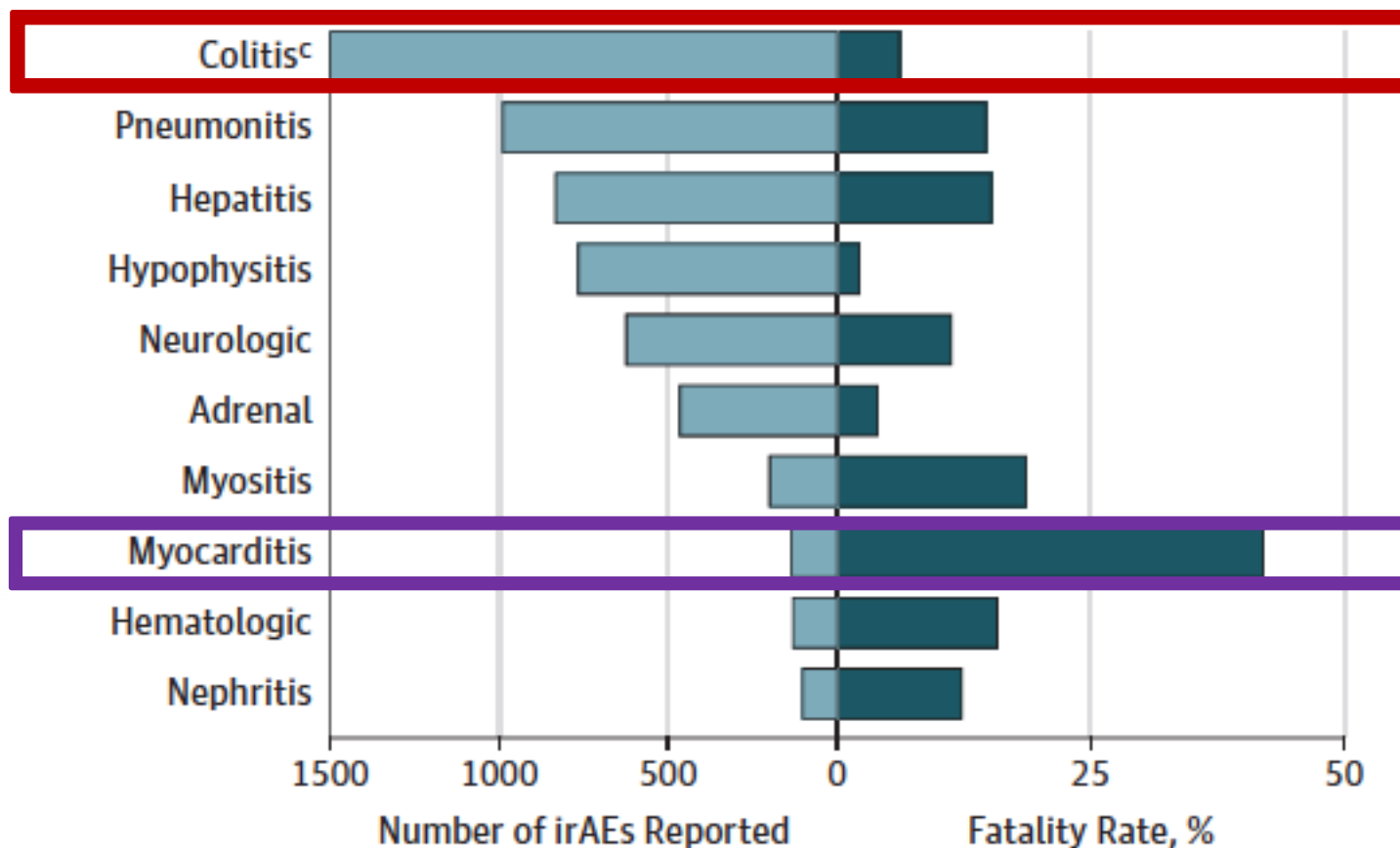
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# Immune side effects are usually delayed in onset, unlike chemotherapy



*Journal of Clinical Oncology* 30(21):2691-2697.

# Colitis was the most common serious side effect but Myocarditis was most lethal by percentage



JAMA Oncol. 2018;4(12):1721-1728.

# American Society of Clinical Oncology(ASCO) 2018 Guideline

- Education prior to and throughout and after treatment.
- High level of suspicion for immune side effects
- Grade 2 toxicity: hold immunotherapy and start corticosteroid (0.5-1mg/kg).
- Grade 3 toxicity: hold and start higher dose corticosteroid (1-2mg/kg IV). Consider adding infliximab or other immunomodulators if no improvement in 48-72hrs.
- Grade 4 toxicity: similar to grade 3 toxicity management plus permanent discontinuation.

Copyright 2018 by American Society of Clinical Oncology



# Important to Slowly Taper Corticosteroid!

- Need to taper prednisone slowly over 4-6 weeks to prevent relapse.
- Depending on the initial severity of immune side effect, Immunotherapy may be resumed when side effects improve to grade 1 and daily prednisone dose of  $\leq 10\text{mg/day}$

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# Patient Education Video

## What I Need to Know about my Immunotherapy

The Center for Cancer Prevention and Treatment  
St Joseph Hospital, Orange

Courtesy of Enza Nguyen, RN, MSN, ANP-BC

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# Immunotherapy Wallet Card

- Your nurse will give you an 'immunotherapy wallet card'
- Keep this card in your wallet at all times
- Present this card to any urgent care or emergency department
- This card helps any healthcare provider identify you as someone undergoing immunotherapy who needs special follow up and care

## Immunotherapy Wallet Card

### Front

#### IMPORTANT INFORMATION

I am receiving or have received

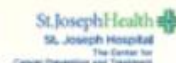
#### IMMUNOTHERAPY.

#### Nurse/Doctor

Please read the information on the reverse side of this card.

Oncologist: \_\_\_\_\_

Contact number: \_\_\_\_\_



### Back

#### ADVICE TO HEALTH CARE PROFESSIONALS

##### Autoimmune side effects:

- Diarrhea and Colitis
- Hepatotoxicities
- Pneumonitis
- Addison's Disease
- Endocrinopathies
- Neuropathies
- Renal Toxicities
- Skin Rashes

##### Required blood tests:

- CBC
- Complete Metabolic Panel
- Random Cortisol/ACTH
- Thyroid function test
- If patient has dyspnea, order Chest CT

Steroids are frequently indicated in the management of side effects and may be given.

# Include in the Past Medical History Section of Medical Record

- Immune-related adverse events can occur even months after treatment has been discontinued.
- Part of the differential diagnosis when patients get sick.

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# Free Tools for immune side effect management: NCCN Guidelines



National  
Comprehensive  
Cancer  
Network®

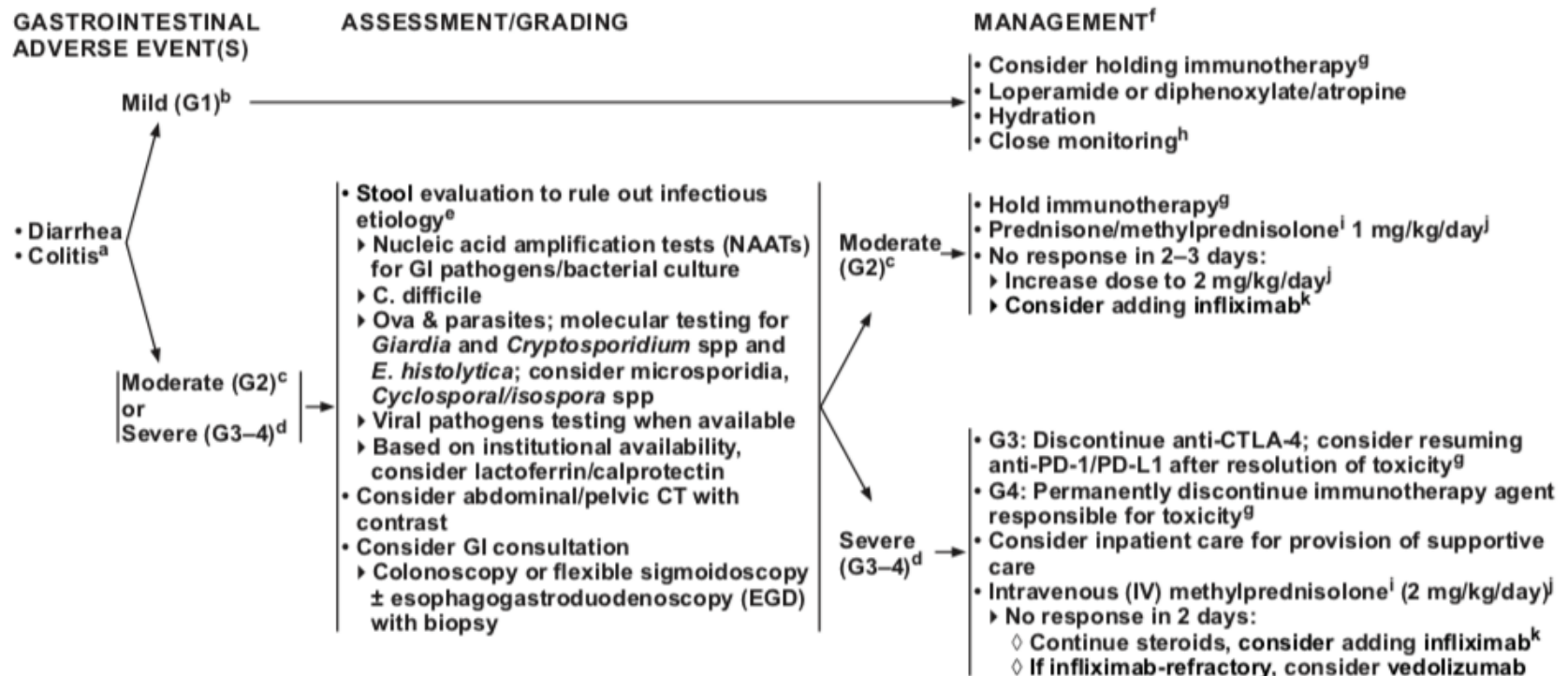
**NCCN Guidelines Version 2.2019**

**Management of Immune Checkpoint Inhibitor-Related Toxicities**

[NCCN Guidelines Index](#)

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[Discussion](#)



[www.nccn.org](http://www.nccn.org)

# Free Tools for immune side effect management: ONCOASSIST



[www.oncoassist.com](http://www.oncoassist.com)

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# Conclusion

- Immune Checkpoint Inhibitors have revolutionized Cancer treatment, and the use is expected to grow over time.
- Immune side effects are usually manageable with prompt recognition and corticosteroid use.
- Immune side effects can occur even after treatment as been discontinued.
- Adherence to guidelines optimize immune side effects management.

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